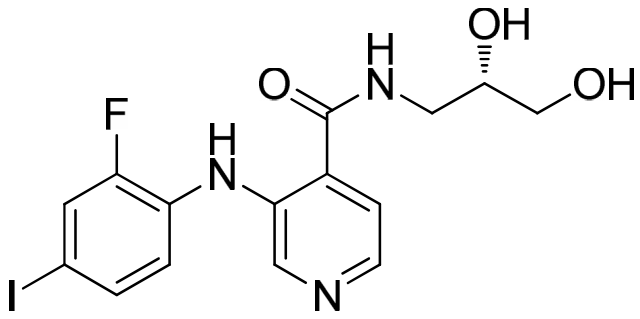
AS703026

SYN-1190



(S)-N-(2,3-dihydroxypropyl)-3-((2-fluoro-4-iodophenyl)amino)isonicotinamide

CAS Registry No.: 1236699-92-5

Smiles String:
IC1=CC(F)=C(NC2=CN=CC=C2C(NC[C@H](O)CO)=O)C=C1

Molecular Weight: 431.2

Molecular Formula: C15H15FIN3O3

Lot Number: Refer to vial

1H-NMR: Available on request

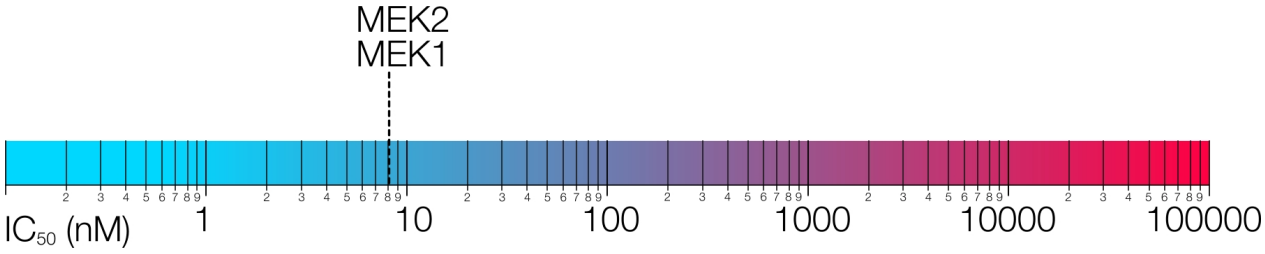
HPLC (Purity): > 95.0% @ 254 nm

ES-MS: Available on request

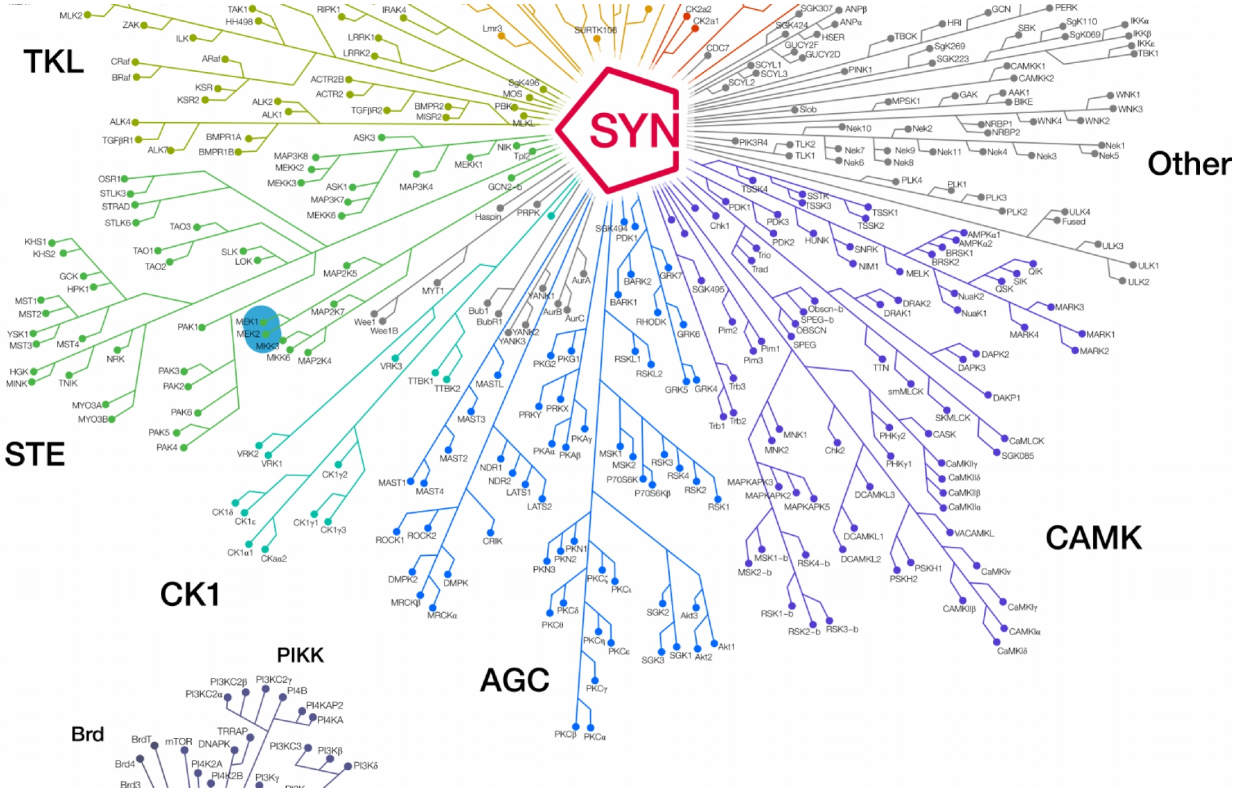
Description:

AS703026 is a novel, selective, non-competitive, orally bioavailable MEK1/2 inhibitor with experimental IC50 values of 5-11 nM. In use on multiple myeloma cells (MM), AS703026 inhibited growth and survival of MM cells and cytokine-induced osteoclast differentiation more potently (~10X) than AZD6244. Inhibition of proliferation induced by AS703026 was mediated by G0-G1 cell cycle arrest and was accompanied by reduction of MAF oncogene expression. AS703026 further induced apoptosis via caspase 3 and Poly ADP ribose polymerase (PARP) cleavage in MM cells, both in the presence or absence of bone marrow stromal cells (BMSCs). Importantly, AS703026 sensitized MM cells to a broad spectrum of conventional (dexamethasone, melphalan), novel or emerging (lenalidomide, perifosine, bortezomib, rapamycin) anti-MM therapies. Significant tumour growth reduction in AS703026- vs. vehicle-treated mice bearing H929 MM xenograft tumours correlated with downregulated pERK1/2, induced PARP cleavage, and decreased microvessels in vivo. Moreover, AS703026 (<200 nmol/l) was cytotoxic against the majority of tumour cells tested from patients with relapsed and refractory MM (84%), regardless of mutational status of RAS and BRAF genes. Importantly, BMSC-induced viability of MM patient cells was similarly blocked within the same dose range.

Biological Activity



Kinome Mapping



Shipping and Storage Temperature

Shipping:
Ambient

Storage:
2 years -20C, Powder 1 month, -4C in DMSO, More than one month -80C in DMSO

Solubility

DMSO 86mg/mL, Ethanol < 1mg/mL

Preparing Stock Solutions

Stock Solution (1ml DMSO)	1mM	10mM	20mM	50mM
Mass(mg)	0.4312	4.3120	8.6240	21.5600

References

1. Kim K, Kong SY, Fulciniti M, Li X, Song W, Nahar S, Burger P, Rumizen MJ, Podar K, Chauhan D, Hideshima T, Munshi NC, Richardson P, Clark A, Ogden J, Goutopoulos A, Rastelli L, Anderson KC, Tai YT. Blockade of the MEK/ERK signalling cascade by AS703026, a novel selective MEK1/2 inhibitor, induces pleiotropic anti-myeloma activity in vitro and in vivo. Br J Haematol. 2010 May;149(4):537-49. doi: 10.1111/j.1365-2141.2010.08127.x. Epub 2010 Mar 12. PubMed PMID: 20331454; PubMed Central PMCID: PMC3418597.

Ordering Information

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